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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/730,334	12/08/2003	Stewart D. Lyman	3191-A	3293

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IMMUNEX CORPORATION
LAW DEPARTMENT
1201 AMGEN COURT WEST
SEATTLE, WA 98119

EXAMINER	
GAMBEL, PHILLIP	
ART UNIT	PAPER NUMBER
1644	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	01/18/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/730,334	LYMAN ET AL.	
	Examiner	Art Unit	
	Phillip Gambel	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 November 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-25* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) _____ is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Given that USPTO records indicate that Lyman is the first-named inventor, applicant is invited to indicate Lyman rather than Nash as the first inventor in communications filed in the Office to avoid any confusion concerning paper matching. For example, see Nash et al. is employed in the header of applicant's communications before the Office.

2. Applicant's amendment, filed 11/6/06, has been entered. Claims 4 and 13 have been amended.

Claims are pending 1-25 are pending.

Applicant's election of the species (A) autologous cells, (B) species of bone marrows as a source of hemopoietic cells and radiotherapy as the form of a nonmyeloablative conditioning regimen in the Response to Restriction Requirement, filed 11/6/06, is acknowledged.

Upon reconsideration in reviewing the prosecution in the prior art, including co-inventors own patent document, all of the current pending claims are under consideration in the interest of compact prosecution.

Applicant is reminded to provide a Listing of the Claims with the proper Status Identifiers, given the consideration of all pending claims.

Claims 1-25 are pending and under consideration in the instant application.

3. The filing date of the instant claims appears to be the filing date of priority USSN 60/431,266.

4. The application is required to be reviewed and all spelling, TRADEMARKS, and like errors corrected.

Trademarks should be capitalized or accompanied by the ® or ™ symbol wherever they appear and be accompanied by the generic terminology. Although the use of trademarks is permissible in patent applications, the proprietary nature of the trademarks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

Appropriate corrections are required.

5. Claims 1-25 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1-25 are indefinite in that the preamble of the independent claims recite "a method" only in the absence of therapeutic endpoint, thereby failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. One of ordinary skill in the art would not be reasonably apprised of the metes and bounds of the invention.

Applicant is reminded that the amendment must point to a basis in the specification so as not to add any new matter. See MPEP 714.02 and 2163.06

6. The following is a quotation of the first paragraph of 35 U.S.C. § 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 3, 10 and 19 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention

In vitro and animal model studies have not correlated well with in vivo clinical trial results in patients. Since the therapeutic indices of biopharmaceutical drugs such as cytokines and growth factors can be species- and model-dependent, it is not clear that reliance on the disclosed hemopoietic growth factors and cytokines accurately reflects the relative ability or efficacy of the claimed methods to employ "any cytokine or growth factor" in the engraftment of hemopoietic stem cells.

Pharmaceutical therapies in the absence of in vivo clinical data are unpredictable for the following reasons; (1) the protein may be inactivated before producing an effect, i.e. such as proteolytic degradation, immunological inactivation or due to an inherently short half-life of the protein; (2) the protein may not reach the target area because, i.e. the protein may not be able to cross the mucosa or the protein may be adsorbed by fluids, cells and tissues where the protein has no effect; and (3) other functional properties, known or unknown, may make the protein unsuitable for in vivo therapeutic use, i.e. such as adverse side effects prohibitive to the use of such treatment.

See page 1338, footnote 7 of Ex parte Aggarwal, 23 USPQ2d 1334 (PTO Bd. Pat App. & Inter. 1992).

Given the highly pleiotropic effects of cytokines and growth factors, the specification does not adequately teach how to effectively to use any cytokine or growth factor to aid in the engraftment of hemopoietic stem cells in order to reach an appropriate beneficial therapeutic endpoint in humans. The specification does not teach how to extrapolate data obtained from various in vitro or in vivo observations as well as clinical experience with certain known hemopoietic cytokines and growth factors to the development of effective methods of engrafting hemopoietic stem cells with any cytokine or growth factor as broadly encompassed by the claimed invention and consistent with the disclosure of the known hemopoietic cytokines and growth factors at the time the invention was made as disclosed on page 4 and 45-46, overlapping paragraph of the instant specification.

In view of the lack of predictability of the art to which the invention pertains the lack of established clinical protocols for effective methods to make and use any growth factor or cytokine in therapies comprising the engraftment of hemopoietic stem cells, undue experimentation would be required to practice the claimed methods with a reasonable expectation of success, absent a specific and detailed description in applicant's specification of how to effectively practice the claimed methods and absent working examples providing evidence which is reasonably predictive that the claimed methods are effective for engrafting hemopoietic stem cells with any cytokine or growth factor.

Applicant is invited to amend the claims to amend the claims to recite the appropriate hemopoietic cytokines and growth factors that aid in the engraftment of hemopoietic stem cells and supported by the instant specification as-filed.

8. The following is a quotation of the appropriate paragraphs of 35 U.S.C. §102 that form the basis for the rejections under this section made in this Office Action:

A person shall be entitled to a patent unless --

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

9. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office Action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

10. Claims 1-25 are rejected under 35 U.S.C § 102(b) as being anticipated by Mardiney et al. (U.S. Patent No. 6,103,694) (see entire document).

Mardiney et al. teach methods of engrafting donor mammalian hemopoietic pluripotent stem cells, including bone marrow and peripheral blood sources (e.g. see column 2, lines 41-51) by administering hemopoietic growth factors, including Flt3-L as well as other known hemopoietic growth factors prior to, concurrent and after transplantation of hemopoietic stems cells (e.g., see column 3, paragraphs 1-2 and column 5, paragraphs 1-4) with a nonmyeloablative conditioning regimen, including low dosage radiation (e.g., from about 10 – 500 Gy) (e.g., see column 1, lines 44-53; column 3, paragraph 3 and 5 as well as Summary of the Invention) for both autologous and allogeneic hemopoietic stem cell transplantation for a variety of disease indications, including numerous hemopoietic-related diseases (e.g., see, see column 4, paragraphs 1-3). Given the transplantation of autologous or allogeneic hemopoietic pluripotent stem cells, the prior art teaches adoptive immunotherapeutic regimens. Given the teachings of administering radiomimetics (e.g., see columns 3-4,overlapping paragraph) as well as the conventional use of immunosuppressive compounds in transplantation (e.g. se Background of the Invention and column 2, lines 65-67), the prior art also contemplates the administration of "one or more immunosuppressants".

It does not appear that the claim language or limitations result in a manipulative difference in the method steps when compared to the prior art disclosure

Applicant is reminded that no more of the reference is required than that it sets forth the substance of the invention. The claimed functional limitations would be inherent properties of the prior art methods of engrafting donor mammalian hemopoietic pluripotent stem cells with Flt3-L and other hemopoietic cytokines with nonmyeloablative regimens, including nonmyeloablative radiation would be inherent properties of the referenced antibodies, including the LM609 antibody specificity and inherent properties of the referenced methods.

11. Claims 1-25 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Lyman et al. (U.S. Patent No. 5,843,423) in view of Mardiney et al. (U.S. Patent No. 6,103,694) and Sykes et al. (U.S. Patent No. 6,558,662).

Lyman et al. teach the same or nearly the same methods of hemopoietic cell transplantation by administering Flt3-L compositions and hemopoietic growth factors, sources of autologous or allogeneic stem / progenitor cells, modes of administration for the same or nearly the same therapeutic regimens and patient populations as the instant disclosure (see entire document, including Summary of the Invention, Detailed Description of the Invention and Claims).

Although Lyman et al. teach cytoreductive regimens, Lyman et al. also acknowledge complications associated with standard immunosuppression / myelosuppression at the time the invention was made (e.g. see Background of the Invention, particularly column 2, paragraphs 2-3).

As noted above, in addition to the teachings of Mardiney et al. on methods of engrafting donor mammalian hemopoietic pluripotent stem cells, including bone marrow and peripheral blood sources (e.g. see column 2, lines 41-51) by administering hemopoietic growth factors, including Flt3-L as well as other known hemopoietic growth factors prior to, concurrent and after transplantation of hemopoietic stems cells (e.g., see column 3, paragraphs 1-2 and column 5, paragraphs 1-4) for both autologous and allogeneic hemopoietic stem cell transplantation for a variety of disease indications, including numerous hemopoietic-related diseases (e.g., see, see column 4, paragraphs 1-3) and the conventional use of immunosuppressive compounds in transplantation (e.g. se Background of the Invention and column 2, lines 65-67),

Mardiney et al. also teach the advantages of including a nonmyeloablative conditioning regimen, including low dosage radiation (e.g., from about 10 – 500 Gy) (e.g., see column 1, lines 44-53; column 3, paragraph 3 and 5 as well as Summary of the Invention).

Other than administering Flt3-L, yet in a similar fashion to both Lyman et al. and Mardiney et al. above concerning methods of transplanting hemopoeitic stem cells,

Sykes et al. teach the same or nearly the same methods of hemopoietic cell transplantation, stem cell compositions, hemopoietic growth factors or cytokines, sources of autologous or allogeneic stem / progenitor cells, modes of administration for the same or nearly the same therapeutic regimens and patient populations, including conventional immunosuppression as encompassed by the instant disclosure and instant claims (see entire document, including Summary of the Invention, Detailed Description of the Invention and Claims).

Further, Sykes et al. also teach nonmyeloablative regimens in the engraftment of hemopoietic stem cells at the time the invention was made, including nonmyeloablative radiation (e.g., see Summary of the Invention, including column 1, lines, 58-65; column 2, lines 27-28; Detailed Description of the Invention, including column 6, paragraph 3; column 10, paragraphs 2, 5 and 7, Discussion on columns 31-32 and Reference 21 on column 34, lines 1-6).

Generally, differences in modes of administration and dosage ranges of therapeutic agents will not support the unobviousness of the claimed methods, unless the modes and dosages are deemed to be critical and unobvious over the prior art. "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." In re Aller, 105 USPQ 233, 235 (CCPA 1955).

Also, a particular parameter must first be recognized as a result-effective variable, i.e., a variable which achieves a recognized result, before the determination of the optimum or workable ranges of said variable might be characterized as routine experimentation. In re Antonie, 195 USPQ 6 (CCPA 1977).

In addition to the modes of administration and dosage ranges described by the prior art, a person of ordinary skill in the art would have recognized that engrafting hemopoietic stem cells with hemopoietic cytokines such as Flt3-L with known methods of nonmyeloablative and immunosuppressive regimens in transplanting such cells, including in certain circumstances lymphoid cells as well as hemopoietic stem cells would have included the various modes of administration and dosages encompassed by the claimed methods in order to meet the needs of the patients to achieve effective therapeutic regimens and maintaining engraftment of the hemopoietic stem cells and their progeny in the transplant recipient consistent with the prior art methods and the instant disclosure at the time the invention was made.

It does not appear that the claim language or limitations result in a manipulative difference in the method steps when compared to the prior art disclosure

One of ordinary skill in the art at the time the invention was made would have been motivated to employ nonmyeloablative radiotherapy in the referenced and known methods of engrafting hemopoietic stem cells, including the use of hemopoietic cytokines or growth factors such as Flt3-L, given the clear teachings of the prior art references of the cytotoxicity and of the complications of myeloablative regimens at the time the invention was made. Further, combination therapies were a common practice at the time the invention was made and nonmyeloablative regimens such as that taught by Mardiney et al. and Sykes et al. were taught in the context of engrafting hemopoietic stem cell therapeutic regimens at the time the invention was made. Therefore, a person of ordinary skill in the art would have a reasonable expectation of success at the time the invention was made.

From the teachings of the references, it was apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

12. It is noted that applicant has a number of copending applications and U.S. Patents which are drawn to methods of administering Flt3-L in the context of engrafting hemopoietic stem cells, generally in the absence of nonmyeloablative regimens.

However, it is not readily apparent whether the claims were subject to restriction and whether the claims are subject to double patenting rejections.

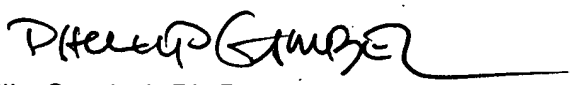
Applicant is invited to clarify which applications should be subject to rejections under the judicially created doctrine of obviousness-type double patenting.

13. No claim is allowed.

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Phillip Gambel whose telephone number is (571) 272-0844. The examiner can normally be reached Monday through Thursday from 7:30 am to 6:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571) 272-0841.

The fax number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



Phillip Gambel, Ph.D., J.D.
Primary Examiner
Technology Center 1600
January 8, 2007